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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,227	11/30/2001	Rosana Kapeller-Libermann	MNI-199	8456

7590 11/15/2004

INTELLECTUAL PROPERTY GROUP
MILLENNIUM PHARMACEUTICALS, INC.
75 SIDNEY STREET
CAMBRIDGE, MA 02139

EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 11/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/001,227	KAPELLER-LIBERMANN ET AL.	
	Examiner	Art Unit	
	Jon M Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *35-66* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 April 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/1/02, 9/7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Alignments*.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group VI (claims 22, 24, and 31, in so far as they are drawn to a method of identifying a compound which binds/modulates COE-2 polypeptides) in the Response and Amendment filed on 07 September 2004 is acknowledged.

2. Applicants note that Group VI should include claims 23, 24, and 31 (in part) rather than claims 22, 24, and 31 (in part), as claim 22 is directed to kits is moot in view of Applicant's cancellation of said claim (filed 07 September 2004)

3. Newly submitted claims 40, 48, 56, and 64 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 40, 48, 56, and 64 (parts (d) and (e) of each claim) are directed to newly introduced assay methods that were not encompassed by the originally claimed assay.

4. The methods of claims 40, 48, 56, and 64 (parts (d) and (e) of each claim) are drawn to patentably distinct methods. Although there are no provisions under the section for "Relationship of Inventions" in M.P.E.P § 806.05 for inventive groups that are directed to different methods, restriction is deemed to be proper because these methods appear to constitute patentably distinct inventions for the following reasons: they utilize different starting materials and methods steps and require non-coextensive searches.

5. Therefore, a search and examination of all the methods of claims 40, 48, 56, and 64 (parts (d) and (e) of each claim) in one patent application would result in an undue burden, since the searches for the Inventions' methods are not co-extensive.

6. Accordingly, claims 40, 48, 56, and 64 as they are drawn to methods of a yeast two-hybrid assay and an assay for lipid metabolism are non-elected by original presentation.

Status of Application, Amendments, and/or Claims

7. The preliminary amendment filed 07 September 2004 has been entered in full. Claims 1-34 are cancelled and claims 35-66 have been added.

Priority

8. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(e), which papers have been placed of record in the file.

Information Disclosure Statement

9. The information disclosure statement filed 01 October 2002 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because copies of references A1-A16 and B1-B6 have not been provided. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

10. The information disclosure statement (IDS) filed 07 September 2004 has been considered by the examiner.

Drawings

11. Applicants are advised that upon issuance of a patent, the complete text of the sequence listing submitted in compliance with 37 C.F.R.§§1.821-1.825 will be published as part of the patent. Therefore, it is unnecessarily redundant to repeat the sequence information in the form of Figures. Applicants should amend the specification to delete any Figures (e.g. Figures 1A and 1B) which consist only of nucleic acid or protein sequences which have been submitted in their entirety in computer readable format (i.e. as SEQ ID NO:'s) and should further amend the specification accordingly to reflect the replacement of the Figure by the appropriate SEQ ID NO:.

Specification

12. The disclosure is objected to because of the following informalities: at page 79, line 17, the Specification states "The results of these analyses are set forth in Figures 5-7". However, the Examiner believes that it should read "Figures 6-8". Appropriate correction is suggested.

Claim Objections

13. Claims 40, 48, 56, and 64 are objected to because of the following informalities: Claims 40, 48, 56, and 64 encompass non-elected inventions, e.g., part (d) a yeast two-hybrid assay, and part (e) an assay for lipid metabolism. Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd paragraph

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 35-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

16. Claims 35, 43, 51, and 59 are indefinite because it is unclear what is meant by the terms "pain disorder" and "pain signaling mechanism". The discussion of "pain disorders" on page 8 of the Specification is noted but vague, is exemplary rather than limiting, fails to breathe life and meaning into the term and thus is insufficient to render the claims definite. Likewise, the phrase "pain signaling mechanism" is unclear as the metes and bounds of this phrase are not defined in the Specification nor are limitations provided in the claim to clearly define said phrase.

17. All remaining claims are rejected for depending from an indefinite claim.

Claim Rejections - 35 USC § 112

18. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

19. Claims 35-66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

20. The claims are drawn to a method of identifying candidate compounds for modulating a pain response. The Specification teaches a polypeptide (COE-2) set forth as SEQ ID NO:2 which, based upon sequence similarity alone, is asserted to be a carboxylesterase (See, for example, page 7, lines 14-21 and Figures 3-5). The Specification asserts that COE-2 is useful in regulating a variety of cellular processes including metabolism of various lipid and fatty acid compounds which are further asserted to be involved in pain and/or inflammation signaling (See pages 1-2). The Specification asserts that COE-2 molecules are useful as therapeutic agents for the treatment of pain (See page 8, lines 8-25, for example), thus, modulators of the COE-2 protein are beneficial for modulating a pain response.

21. The specification as filed does not provide guidance or examples that would enable a skilled artisan to use the disclosed methods of identifying a candidate compound for modulating a pain disorder or modulating a pain signaling mechanism. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

22. The only evidence in the Specification is a teaching that the gene encoding the COE-2 polypeptide is highly expressed in tissues which contain afferent neurons, particularly the brain and spinal cord (See page 7, line 36 – page 8, line 8). However, the person of ordinary skill in the art would not consider the expression pattern alone would be predictive of involvement of COE-2 in pain signaling. The art teaches that carboxylesterases are found in a wide variety of tissues and appear to be active in the detoxification of foreign compounds, as well as in the regulation of various membrane lipid concentrations (Yamada et al. (1995). "Localization of an isoform of carboxylesterase in rat brain differs from that in human brain." Brain Research 674:175-179; Cited by Applicants). Yamada et al. also teach that, based on the localization of this carboxylesterase to brain regions involved in the medial pain system, carboxylesterase may play a role in regulating the second messenger pain related signals (See page 178, last paragraph). Furthermore, Mantyh et al. (2002, "Molecular mechanism of cancer pain." Nature Reviews 2:201-209) teach that nociceptors, specialized sensory neurons that function to detect and convert environmental stimuli that are perceived as harmful into electrochemical signals that are transmitted to the central nervous system, express a diverse repertoire of receptors to detect a wide range of stimulus modalities. One such example is the vanilloid receptor, which has been disclosed in the art to detect heat as well as acids, extracellular protons, and lipid metabolites (See page 202, for example). Lastly, Julius et al. (2001, "Molecular mechanisms of nociception." Nature 413:203-210) teach the vanilloid receptor can be activated by polyunsaturated fatty acids or other lipid metabolites. Examples of these such as the endogenous cannabinoid receptor agonist anandamide, or lipoxygenase products of arachidonic acid metabolism are weak as agonists of the vanilloid receptor. They further teach that since the

physiological setting in which these molecules (lipids and lipid metabolites) are likely to act as vanilloid receptor agonists is one involving inflammation, it is necessary to determine whether these lipid metabolites act synergistically with other pro-inflammatory agents, such as bradykinin, NGF, or protons to facilitate vanilloid receptor gating (See especially page 208).

23. Furthermore, even if the tissue distribution of COE-2 mRNA (See page 78, line 33 – page 79, line 22; Figures 6-8) was predictive of involvement of COE-2 in pain signaling, the specification as filed provides no nexus between COE-2 and any "pain disorder". A "pain disorder" can be interpreted to mean any disorder that causes pain, or it can be interpreted to mean any disorder where pain is either positively or negatively affected. Furthermore (and in view of the 112¶2 rejection *supra*) pain is a complex experience that involves not only the transduction of noxious stimuli as addressed above, but also involves cognitive and emotional processing by the brain involving separate forebrain mechanisms (See, for example Casey (1999). "Forebrain mechanisms of nociception and pain: analysis through imaging." Proc. Natl. Acad. Sci. USA 96:7668-7674).

24. Therefore, the person of ordinary skill in the art would not be able to use the method to identify a candidate compound for modulating a pain disorder or a pain signaling mechanism because there is no reasonable expectation that compounds identified by the method would have the claimed property of being a candidate for modulating a "pain disorder", and if so, what "pain disorder". In order to practice the invention using the specification and the state of the prior art as outlined above, the quantity of experimentation required to practice the invention as claimed would be undue.

Claim Rejections - 35 USC § 102

25. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

26. Claims 35-36, 38-44, 46-52, 54-60, and 62-66 are rejected under 35 U.S.C. 102(e) as being anticipated by Baughn et al. (WO 02/12467 A2, priority date 4 August 2000, citation #BA on the IDS filed 07 September 2004). Baughn et al. teach a DME 10 polypeptide (SEQ ID NO :10) that has 100% sequence identity to SEQ ID NO:2 of the instant Application (See attached sequence alignment) that they disclose as a carboxylesterase (See page 48, lines 13-20). Baughn et al. also teach that the DME 10 polypeptide may be used to screen for compounds that act as an agonist of DME 10 (See page 28, line 26 – page 29, line 5); compounds that act as antagonists of DME 10 (See page 29, lines 6-18); and compounds that bind DME 10 (See page 61, lines 22-25). Baughn et al. teach examples of compounds to be screened include antibodies, oligonucleotides, protein, or small molecules (See page 61, lies 22-25). Baughn et al. teach the DME 10 polypeptide used in the assays can be comprised in a cell, membrane bound, in solution, or affixed to a solid support (See page 61, line 31 – page 62, line 10). Baughn et al. teach various methods for the detection of binding including direct binding detected by fluorophore, radioisotope, enzyme conjugate, or other detectable label. Baughn et al. also teach the detection

of the binding of DME 10 to the test compound in the presence of a labeled competitor (See page 62, lines 4-8) and by immuno assay (See page 61, lines 2-4). Baughn et al. also teach the DME 10 polypeptide used in the assays further comprising a heterologous moiety (See page 61, lines 2-4). Lastly, Baughn et al. teach screening compounds that modulate the activity of DME 10. Although they are silent as to the specific type of activity they are measuring, any activity attributed to DME 10 (a carboxylesterase) would be considered carboxylesterase activity.

27. Therefore, Baughn et al. teach all the limitations of claims 35-36, 38-44, 46-52, 54-60, and 62-66.

Summary

28. No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback, Ph.D.** can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JML
November 9, 2004

LORRAINE SPECTOR
PRIMARY EXAMINER

FT /note= "esterase carboxylase serine alpha esterase
FT domain"
FT Domain 366. .474
FT /note= "carboxylesterase signal serine liver glycoprotein
FT domain"
FT Domain 395. .554
FT /note= "acetylcholinesterase domain"
FT Domain 415. .573
FT /note= "esterase domain"
FT Domain 487. .569
FT /note= "esterase hydrolase domain"
FT Domain 536. .580
FT /note= "carboxylesterase hydrolase precursor domain"
XX
PN WO200244357-A2.
XX
PD 06-JUN-2002.
XX
PF 30-NOV-2001; 2001WO-US045356.
XX
PR 30-NOV-2000; 2000US-0250929P.
XX
PA (MILL-) MILLENNIUM PHARM INC.
XX
PI Kapeller-Libermann R, Silos-Santiago I;
XX
DR WPI; 2002-537452/57.
DR N-PSDB; ABN84189.
XX
PT Novel isolated human carboxylesterase-2 family member polypeptide, 18903,
PT useful for treating inflammatory disorders, pain disorders, tumor and
PT cancer.
XX
PS Claim 12; Page 122-123; 129pp; English.
XX
CC The present sequence is the protein sequence of human carboxylesterase-2
CC (COE-2), a novel carboxylesterase family member. COE-2 participates in
CC the metabolism of various lipid and fatty acid compounds which are
CC involved in pain and/or inflammation signalling. It is highly expressed
CC in tissues which contain afferent neurons, particularly brain and spinal
CC cord tissue. Homology searches against different databases identified a
CC number of characteristic domains and motifs in the COE-2 amino acid
CC sequence. The invention provides COE-2 nucleic acid molecules, antisense
CC nucleic acid molecules, recombinant expression vectors, host cells,
CC transgenic animals, isolated COE-2 proteins, fusion proteins, antigenic
CC peptides and anti-COE-2 antibodies. COE-2 binding substances are used in
CC claimed methods of identifying subjects having, or at risk of developing,
CC an inflammatory or pain disorder. Compounds capable of treating an
CC inflammatory or pain disorder are identified from their ability to
CC modulate COE-2 nucleic acid expression or COE-2 polypeptide activity.
CC Modulator compounds are used in a claimed method of treating an
CC inflammatory or pain disorder. Carboxylesterase-associated pain disorders
CC include hyperalgesia, pain associated with musculoskeletal disorders and
CC pain associated with surgery, rheumatoid arthritis, viral infection,
CC allergic reaction, asthma, pancreatitis, somatoform disorders,
CC fibromyalgia syndrome, etc. Carboxylesterase-associated inflammatory
CC disorders include viral infection, ulcerative colitis, Crohn's disease,
CC asthma, rheumatoid arthritis, scleroderma, psoriasis, inflammatory bowel
CC disorder, peritonitis, chronic obstructive pulmonary disease, lung
CC inflammation, asthma, appendicitis, septic shock, nephritis, amyloidosis,
CC chronic bronchitis, sarcoidosis, scleroderma, lupus, polymyositis,
CC Reiter's syndrome, psoriasis, pelvic inflammatory disease, inflammatory
CC breast disease, orbital inflammatory disease. Other carboxylesterase-
CC associated disorders include tumours, cancer, aberrant blood pressure,
CC aberrant blood clotting, misregulation of various reproductive functions
CC e.g. induction of labour, and misregulation of the sleep/wake cycle. COE-
CC 2 nucleic acids and polypeptides are also useful in screening assays,
CC detection assays (e.g., chromosomal mapping, tissue typing, forensic
CC biology) and predictive medicine (e.g., diagnostic assays, prognostic
CC assays, monitoring clinical trials and pharmacogenomics)
XX
SQ Sequence 584 AA;

Query Match 100.0%; Score 3112; DB 5; Length 584;
Best Local Similarity 100.0%; Pred. No. 1.9e-286;
Matches 584; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 MPSTVLPSTVLPSLLPTAGAGWSMRWILCWSLTLCLMAQTALGALHTKRPQVVTKYGTLQ 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MPSTVLPSTVLPSLLPTAGAGWSMRWILCWSLTLCLMAQTALGALHTKRPQVVTKYGTLQ 60

Qy         61 GKQMHVGKTPIQVFLGVPFSRPPLGILRFAPPEPPPEPWKGIRDATTYPPGCLQESWGQLA 120
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Qy        121 SMYVSTRERYKWLRFSEDCLYLNVYAPARAPGDPQLPVMVWFPGGAFIVGAASSYEGSDL 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 SMYVSTRERYKWLRFSEDCLYLNVYAPARAPGDPQLPVMVWFPGGAFIVGAASSYEGSDL 180

Qy        181 AAREKVVLVFLQHRLGIFGFLSTDDSHARGNWGLLDQMAALRWVQENIAAFGGDPGNVTL 240
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Qy        241 FGQSAGAMSISGLMMSPLASGLFHRAISQSGTALFRLFITSNPLKVAKKVAHLAGCNHNS 300
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Db        241 FGQSAGAMSISGLMMSPLASGLFHRAISQSGTALFRLFITSNPLKVAKKVAHLAGCNHNS 300

Qy        301 TQILVNCLRALSGTKVMRVSNKMRFLQLNFQRDPEEIIWSMSPVVDGVVIPDDPLVLLTQ 360
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Db        301 TQILVNCLRALSGTKVMRVSNKMRFLQLNFQRDPEEIIWSMSPVVDGVVIPDDPLVLLTQ 360

Qy        361 GKVSSVPYLLGVNNLEFNWLLPYIMKFPLNRQAMRKETITKMLWSTRTLLNITKEQVPLV 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 GKVSSVPYLLGVNNLEFNWLLPYIMKFPLNRQAMRKETITKMLWSTRTLLNITKEQVPLV 420

Qy        421 VEEYLDNVNEHDWKMLRNRMMDIVQDATFVYATLQTAHYHRDAGLPVYLYEFEHHARGII 480
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Db        421 VEEYLDNVNEHDWKMLRNRMMDIVQDATFVYATLQTAHYHRDAGLPVYLYEFEHHARGII 480

Qy        481 VKPRTDGADHGDEMYFLFGGPFATGLSMGKEKALSLQMMKYWANFARTGNPNDGNLPCWP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 VKPRTDGADHGDEMYFLFGGPFATGLSMGKEKALSLQMMKYWANFARTGNPNDGNLPCWP 540

Qy        541 RYNKDEKYLQLDFTTRVGMKLKEKKMAFWMSLYQSQRPEKQRQF 584
              |||||||||||||||||||||||||||||||||||||||||||
Db        541 RYNKDEKYLQLDFTTRVGMKLKEKKMAFWMSLYQSQRPEKQRQF 584
```

RESULT 2
AAE21052
ID AAE21052 standard; protein; 584 AA.
XX
AC AAE21052;
XX
DT 01-JUL-2002 (first entry)
XX
DE Human drug metabolising enzyme (DME-10) protein.
XX
KW Human; drug metabolising enzyme; cell proliferative disorder; metabolic;
KW autoimmune; inflammatory; developmental; gastrointestinal; hypergonadal;
KW pancreatic; endocrine; eye; dermatitis; Addison's disease; antilipaemic;
KW acquired immunodeficiency syndrome; AIDS; glomerulonephritis; anorectic;
KW diabetes; atherosclerosis; adult respiratory distress syndrome; anaemia;
KW Grave's disease; thyroiditis; Crohn's disease; infection; anticoagulant;
KW systemic lupus erythematosus; cirrhosis; psoriasis; epilepsy; gastritis;
KW cataract; hypopituitarism; cancer; rheumatoid arthritis; conjunctivitis;
KW cystic fibrosis; peptic ulcer; Wilson's disease; hepatitis; antithyroid;
KW allergy; diarrhoea; thrombosis; obesity; immunostimulant; tranquillizer;
KW infertility; vulnerary; anticonvulsant; gynaecological; laxative; goitre;
KW nootropic; jaundice; trauma; asthma; DME-10; enzyme.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Peptide 1. .43
FT /label= Signal_peptide

FT Protein 44. .584
FT /note= "Mature human DME-10 protein"
FT Domain 137. .147
FT /note= "Carboxylesterase B2 motif"
FT Domain 231. .246
FT /note= "Carboxylesterase B1 motif"
XX
PN WO200212467-A2.
XX
PD 14-FEB-2002.
XX
PF 03-AUG-2001; 2001WO-US024382.
XX
PR 04-AUG-2000; 2000US-0223055P.
PR 11-AUG-2000; 2000US-0224728P.
PR 18-AUG-2000; 2000US-0226440P.
PR 24-AUG-2000; 2000US-0228067P.
PR 31-AUG-2000; 2000US-0230063P.
PR 13-SEP-2000; 2000US-0232244P.
PR 20-SEP-2000; 2000US-0234269P.
XX
PA (INCY-) INCYTE GENOMICS INC.
XX
PI Baughn MR, Bruns CM, Das D, Delegeane AM, Ding L, Elliot VS;
PI Gandhi AR, Griffin JA, Hafalia AJA, Khan FA, Lal P, Lee S, Lu DAM;
PI Lu Y, Patterson C, Ramkumar J, Ring HZ, Sanjanwala MS, Tang YT;
PI Thangavelu K, Thornton M, Tribouley CM, Walia NK, Warren BA, Yang J;
PI Yao MG, Yue H;
XX
DR WPI; 2002-206331/26.
DR N-PSDB; AAD33489.
XX
PT New human drug metabolizing enzyme polypeptide and polynucleotide useful
PT for diagnosing, treating and preventing cell proliferative,
PT autoimmune/inflammatory, endocrine, eye, metabolic and gastrointestinal
PT disorders.
XX
PS Claim 54; Page 154-156; 179pp; English.
XX
CC The invention relates to an isolated human drug metabolising enzyme (DME)
CC polypeptide or a biologically active or immunogenic fragment of DME. DME
CC is useful for diagnosis, treatment and prevention of cell proliferative,
CC autoimmune/inflammatory, developmental, endocrine, eye, metabolic and
CC gastrointestinal disorders including live disorders. Autoimmune/
CC inflammatory disorders include acquired immunodeficiency syndrome (AIDS),
CC adult respiratory distress syndrome, Addison's disease, atherosclerosis,
CC allergies, anaemia, asthma, autoimmune haemolytic anaemia, autoimmune
CC thyroiditis, Crohn's disease, atopic dermatitis, diabetes mellitus,
CC glomerulonephritis, rheumatoid arthritis, systemic lupus erythematosus,
CC ulcerative colitis, uveitis, viral, bacterial, protozoal, parasitic,
CC fungal, helminthic infections and trauma. Cell proliferative disorders
CC include cancer, arteriosclerosis, cirrhosis and psoriasis; developmental
CC disorders include epilepsy and cataract; and endocrine disorders include
CC disorders of hypothalamus/pituitary, disorders associated with
CC hypopituitarism, including diabetes insipidus, hypogonadism, disorders
CC associated with hypothyroidism including goitre, Grave's disease,
CC pancreatic disorders such as diabetes mellitus, disorders associated with
CC adrenals, disorders associated with gonadal steroid hormones such as
CC endometriosis, infertility, hypergonadal disorders and gynaecomastia.
CC Disorders of the eye include conjunctivitis and macular degeneration and
CC metabolic disorders include diabetes, cystic fibrosis, obesity and
CC hypocalcaemia. Gastrointestinal disorders include gastritis, peptic
CC ulcer, hepatitis, constipation, diarrhoea, jaundice, Wilson's disease,
CC thrombosis and hepatic tumours. DME gene is useful in gene therapy. The
CC present sequence is human DME-10 protein
XX
SQ Sequence 584 AA;

Query Match 100.0%; Score 3112; DB 5; Length 584;
Best Local Similarity 100.0%; Pred. No. 1.9e-286;
Matches 584; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 MPSTVLPSTVLPSLLPTAGAGWSMRWILCWSLTLCLMAQTALGALHTKRPQVVTKYGTLQ 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MPSTVLPSTVLPSLLPTAGAGWSMRWILCWSLTLCLMAQTALGALHTKRPQVVTKYGTLQ 60

Qy         61 GKQMHVGKTPIQVFLGVPFSRPPLGILRFAPPEPPEPWKGIRDATTYPPGCLQESWGQLA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GKQMHVGKTPIQVFLGVPFSRPPLGILRFAPPEPPEPWKGIRDATTYPPGCLQESWGQLA 120

Qy        121 SMYVSTRERYKWLRFSEDCLYLNVYAPARAPGDPQLPVMVWFPGGAFIVGAASSYEGSDL 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 SMYVSTRERYKWLRFSEDCLYLNVYAPARAPGDPQLPVMVWFPGGAFIVGAASSYEGSDL 180

Qy        181 AAREKVVLVFLQHRLGIFGFLSTDDSHARGNWGLLDQMAALRWVQENIAAFGGDPGNVTL 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 AAREKVVLVFLQHRLGIFGFLSTDDSHARGNWGLLDQMAALRWVQENIAAFGGDPGNVTL 240

Qy        241 FGQSAGAMSISGLMMSPLASGLFHRAISQSGTALFRLFITSNPLKVAKKVAHLAGCNHNS 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 FGQSAGAMSISGLMMSPLASGLFHRAISQSGTALFRLFITSNPLKVAKKVAHLAGCNHNS 300

Qy        301 TQILVNCLRALSGTKVMRVSNKMRFLQLNFQRDPEEIIWSMSPVVDGVVIPDDPLVLLTQ 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 TQILVNCLRALSGTKVMRVSNKMRFLQLNFQRDPEEIIWSMSPVVDGVVIPDDPLVLLTQ 360

Qy        361 GKVSSVPYLLGVNNLEFNWLLPYIMKFPLNRQAMRKETITKMLWSTRTLLNITKEQVPLV 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 GKVSSVPYLLGVNNLEFNWLLPYIMKFPLNRQAMRKETITKMLWSTRTLLNITKEQVPLV 420

Qy        421 VEEYLDNVNEHDWKMLRNRMMDIVQDATFVYATLQTAHYHRDAGLPVYLYEFEHHARGII 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 VEEYLDNVNEHDWKMLRNRMMDIVQDATFVYATLQTAHYHRDAGLPVYLYEFEHHARGII 480

Qy        481 VKPRTDGADHGDEMYFLFGGPFATGLSMGKEKALSLQMMKYWANFARTGNPNDGNLPCWP 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 VKPRTDGADHGDEMYFLFGGPFATGLSMGKEKALSLQMMKYWANFARTGNPNDGNLPCWP 540

Qy        541 RYNKDEKYLQLDFTTRVGMKLKEKKMAFWMSLYQSQRPEKQRQF 584
              |||||||||||||||||||||||||||||||||||||||||||
Db        541 RYNKDEKYLQLDFTTRVGMKLKEKKMAFWMSLYQSQRPEKQRQF 584
```

RESULT 3
ABG10635
ID ABG10635 standard; protein; 509 AA.
XX
AC ABG10635;
XX
DT 13-FEB-2002 (first entry)
XX
DE Novel human diagnostic protein #10626.
XX
KW Human; chromosome mapping; gene mapping; gene therapy; forensic;
KW food supplement; medical imaging; diagnostic; genetic disorder.
XX
OS Homo sapiens.
XX
PN WO200175067-A2.
XX
PD 11-OCT-2001.
XX
PF 30-MAR-2001; 2001WO-US008631.
XX
PR 31-MAR-2000; 2000US-00540217.
PR 23-AUG-2000; 2000US-00649167.
XX
PA (HYSE-) HYSEQ INC.
XX
PI Drmanac RT, Liu C, Tang YT;
XX
DR WPI; 2001-639362/73.
DR N-PSDB; AAS74822.
XX
PT New isolated polynucleotide and encoded polypeptides, useful in
PT diagnostics, forensics, gene mapping, identification of mutations